

REMARKS

Claims 1, 4, 42, 43, and 45-50 are pending. Claims 1, 4, 42, 43, and 45-50 are rejected under 35 U.S.C. § 112, first paragraph, claim 50 is rejected under 35 U.S.C. § 112, second paragraph, and claims 1, 43, and 45-50 are rejected under 35 U.S.C. § 102(b). Applicants address each of these rejections as follows.

Claim Amendments

Claim 50 has been amended to recite an isolated glycoprotein including a section of a glycosylated human CD55 protein expressed by adenocarcinoma cell line 23132 (DSMZ Accession No. DSM ACC 201), but not by a normal cell, where the glycosylated human CD55 protein has an apparent molecular weight of about 82 kD and where the section of the glycosylated human CD55 protein includes a tumor-specific N-linked glycostructure. Support for this amendment is found, for example, at page 5, lines 7-18, of the English language specification.

In addition, new claims 51-56 have been added. These new claims find support, for example, at page 4, line 15, to page 5, line 6, of the English language specification.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 50

Claim 50 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply

with the written description requirement. In particular, the Office states (page 3):

New claim 50 suggests that a section of the glycoprotein has a molecular weight of about 82 kD ... The specification and new claim 50 are not consistent with regard to the molecular weight.

Applicants submit that claim 50, as amended, is free of this basis for rejection.

Claims 1, 4, 42, 43, and 45-50

The Office rejects claims 1, 4, 42, 43, and 45-50 under 35 U.S.C. § 112, first paragraph, for an asserted lack of written description. The Office states (page 4):

The specification continues to be remiss of information detailing what defines tumor-specific N-linked glycostructure and how one of ordinary skill in the art could identify said structure. There is insufficient guidance regarding the section of the protein that is to have this specific structure.

Applicants disagree.

Claim 1 is directed to an isolated glycoprotein containing the human amino acid primary structure of CD55 and a tumor-specific N-linked glycostructure. Claim 1 further requires the glycoprotein to have an apparent molecular weight of about 82 kD and to be a glycoprotein present on adenocarcinoma cell line 23132, but not on a normal cell.

To fulfill the written description requirement of § 112, the patent specification does not need to describe exactly all the subject matter that is claimed. *In re Daniels*, 114 F.3d 1452, 46 U.S.P.Q.2d 1788 (Fed. Cir. 1998); *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 227 U.S.P.Q. 117 (Fed. Cir. 1985). Rather, the specification must clearly allow a person of ordinary skill in the art to recognize that the inventor has

invented what is claimed. *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473, 45 U.S.P.Q.2d 1498 (Fed. Cir. 1998). In applying this standard, the Federal Circuit has held that the specification must convey with reasonable clarity to a skilled artisan that the inventor "was in possession of the invention" at the time of filing. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). Applicants' specification clearly meets this standard.

As an initial matter, the nucleic acid and amino acid sequences of wild-type CD55 (DAF) were publicly known at the time the present application was filed (see, e.g., Caras et al., U.S. Patent No. 5,763,224, issued June 9, 1998, and entitled "Decay Accelerating Factor (DAF) and Nucleic Acids Encoding It; copy enclosed with Applicants' last reply). In addition, antibodies that recognize the amino acid primary structure of CD55 (DAF) were also available in the art at the time the present application was filed (see, e.g., Hara et al., *Immunol. Lett.* 37:145-152, 1993; copy enclosed with Applicants' last reply). In fact, Karnauchow et al. (*Journal of Virology* 70(8):5143-5152, 1996; hereafter "Karnauchow") cited by the Office in the present Office Action describes an antibody that binds wild-type CD55 (DAF).

The specification also describes a publicly available cell line (human adenocarcinoma cell line 23132) that expresses a glycoprotein having the tumor-specific glycostructure recited in the present claims (see, for example, at page 5, lines 12-18, of the English language text). Applicants note that the Federal Circuit has held that one may

comply with the written description requirement by publicly depositing the biological material. *Enzo Biochem, Inc., v. Gen-Probe Inc.*, 296 F.3d 1316, 63 U.S.P.Q.2d 1609 (Fed. Cir. 2002). As Applicants' specification describes a publicly deposited cell line expressing a glycoprotein encompassed by the present claims, antibodies allowing one skilled in the art to identify this glycoprotein were publicly available, and the sequence of the amino acid primary structure of this glycoprotein was publicly available, there can be no question that Applicants were in possession of the claimed invention at the time of filing.

Further, as shown in Figure 7 of Coyne et al. (*J. Immunology* 149:2906-2913, 1992; "Coyne;" copy enclosed with Applicants' last reply), Applicants note that CD55/DAF only contains one N-linked glycosylation site. Given that the sequence of wild-type CD55 and the location of its single N-linked glycosylation site were publicly known at the time the application was filed, one skilled in the art would recognize which section of CD55 would contain a tumor-specific N-linked glycostructure.

As an additional basis for the written description rejection, the Office asserts (page 5):

The specification submits that the claimed invention reads on "...variants with deletions, insertions and/or substitutions in the amino acid primary structure..." It is not clear how one of ordinary skill in the art could definitely recognize whether or not they were also in possession of Applicants' claimed invention, thereby infringing on Applicants' claimed invention. (citations omitted)

Applicants draw the Office attention to the language of the present independent

claims. The present claims require the isolated glycoprotein to comprise the human amino acid primary structure of CD55 and a tumor-specific glycostructure (claim 1) or a section of a glycosylated human CD55 protein expressed by adenocarcinoma cell line 23132 (DSMZ Accession No. DSM ACC 201), but not by a normal cell, where the glycosylated human CD55 protein has an apparent molecular weight of about 82 kD and where the section of the glycosylated human CD55 protein includes a tumor-specific N-linked glycostructure (claim 50). These claims do not recite variants with deletions, insertions and/or substitutions in the amino acid primary structure of CD55 or in the amino acid primary structure of a section of this protein. Quite to the contrary, the claims are specifically drawn to isolated glycoproteins having the human amino acid primary structure of CD55, or a section of this protein, containing a tumor-specific glycostructure.

The claimed glycoprotein is described throughout the specification, for example, at page 5, lines 7-18, of the English language text. Variants of the claimed glycoprotein are described, for example, at page 5, lines 18-23, of the English language specification.

Here the specification states:

In addition to this 82 kD ... protein, the invention also relates to variants with deletions, insertions and/or substitutions in the amino acid primary structure, which, however, have a glycostructure that is analogous to the natural protein, i.e., tumor-specific and preferably reactive with antibody SC-1. (emphasis added)

While the specification describes additional desirable embodiments, these embodiments are not recited in the present claims. Thus, as the amino acid primary structure of CD55

was publicly known at the time of filing, Applicants submit that one skilled in the art would recognize whether a polypeptide contains the CD55 amino acid primary structure, or a section of this protein, simply by comparing amino acid sequences.

The Office also cites *Lilly* in support of the written description rejection. In particular, the Office states (page 5 - page 6):

In *The Regents [sic] of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus ... "An adequate written description of a DNA... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention."

Applicants submit that their specification provides a written description of the presently claimed invention in sufficient detail to satisfy the standard set by the Federal Circuit in *Lilly*. In particular, *Lilly* specifically states that the written description of a genus of DNA may be achieved by a "recitation of structural features common to members of the genus." *Regents of University of California v. Eli Lilly & Co.*, 119 F.3d 1159, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). The Guidelines for Examination of Patent Applications Under 35 U.S.C. 112 ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) state:

The written description requirement for a claimed genus may be satisfied ... by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled

with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

An applicant shows possession of the claimed invention by describing the claimed invention with all its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). Applicants' specification meets this standard for the presently claimed invention.

The present claims require the isolated polypeptide to have the amino acid primary structure of CD55, or a section of this protein, and a tumor-specific N-linked glycostructure. As noted above, the wild-type CD55 protein and its amino acid primary structure were known at the time the application was filed and the single N-linked glycosylation site was also known. Moreover, as is taught in Applicants' specification, a publicly available cell line expresses a glycoprotein having a tumor-specific glycostructure encompassed by the claims. For all the above reasons, Applicants submit that the combination of structural characteristics recited in the claims are sufficient to show that Applicants were in possession of the claimed glycoprotein at the time the application was filed. The written description rejection should be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 1, 43, and 45-50 are rejected under 35 U.S.C. § 102(b) as being anticipated

by Karnauchow. The Office states (page 7):

Karnauchow discloses a HeLa cell glycoprotein of approximately 75 kDa, see abstract. It is within the purview of the Examiner that this disclosed molecular weight is about 82kD ... The disclosed protein appears to be the same as Applicants thereby inherently possessing a tumor-specific N-linked glycostructure and present on the specified cell line ... the burden of proof is upon Applicants to show an unobvious distinction between the structural and functional characteristics of the glycoprotein and antibody in the claimed invention.

Applicants note that, in the abstract, Karnauchow teaches:

MAB EVR1 identified a HeLa cell glycoprotein of approximately 75 kDa that is attached to the cell membrane by a glycosyl-phosphatidylinositol (GPI) anchor. Decay-accelerating factor (DAF, CD55) is a 70- to 75-kDa GPI-anchored membrane protein ... MAB EVR1 bound to Chinese hamster ovary (CHO) cells constitutively expressing human DAF.

The present claims require the glycoprotein to include not only the amino acid primary structure of CD55 or a section of this protein, but also a tumor-specific N-linked glycostructure. The glycoprotein recited in the claims must have an apparent molecular weight of about 82 kD and be a glycoprotein present on adenocarcinoma cell line 23132, but not on a normal cell. Moreover, dependent claims 43 and 51 require that, if the glycoprotein is present on a cell and bound by an antibody that is specific for the tumor-specific N-linked glycostructure, the cell undergoes apoptosis.

Nowhere does Karnauchow teach that the antigen recognized by EVR1 is a glycoprotein having the amino acid primary structure of CD55, or a section of this protein, and a tumor-specific N-linked glycostructure as required by the present claims.

In fact, the antigen recognized by EVR1 has the molecular weight of wild-type CD55 (70-

75 kD as taught by Karnauchow) and not the approximately 82 kD required by claims. Applicants submit that a protein of 75 kD does not have a molecular weight of about 82 kD.

Moreover, Karnauchow's EVR1 antibody does not specifically bind a CD55 protein with a tumor-specific glycostructure. Karnauchow confirms that the antigen recognized by EVR1 on HeLa cells is CD55 by recombinantly expressing wild-type human DAF (CD55) in Chinese Hamster Ovary (CHO) and murine NIH 3T3 cells. EVR1 binds CHO and 3T3 cells expressing wild-type human DAF (CD55), but not untransfected CHO or 3T3 cells which do not express human DAF (CD55). Based on these results, Karnauchow states (page 5148, right column), "Our data are consistent with the possibility that Mab EVR1 identified DAF (CD55)." Accordingly, Karnauchow concludes that, because EVR1 binds recombinantly expressed wild-type DAF (CD55), the protein bound by EVR1 on HeLa cells is DAF (CD55). Clearly Karnauchow does not describe a tumor-specific isoform of DAF (CD55).

In contrast, the 82 kD isoform of CD55 recited in claims 1 and 50 is a tumor-specific isoform that is not present on normal CD55 expressing cells. The specification teaches that Applicants were able to readily distinguish between proteins of approximately 70 kD and approximately 82 kD (see, e.g., page 28, lines 12-22, of the English language specification). Here the specification teaches:

By altering stringency (1M of NaCl) and with use of membrane preparations, it was possible to detect other proteins with approximately 70 kD and approximately 82 kD (Figure 1a, trace 1).

Figure 1A shows a Western blot with several distinct protein bands. The 70 kD band is clearly distinguished from the 82 kD band.

Moreover, claim 1 not only requires the glycoprotein to have an apparent molecular weight of about 82 kD, but to also be a glycoprotein present on adenocarcinoma cell line 23132, but not on a normal cell. This embodiment is illustrated in the specification, for example, at page 3, line 25, to page 4, line 3. The specification teaches:

The cellular receptor of antibody SC-1 is an isoform of the protein CD55/DAF that is specific for tumor cells, especially for gastric carcinoma cells, which does not occur in normal tissue. (citations omitted)

In sum, Karnauchow does not teach a glycoprotein having all the features of the glycoprotein encompassed by claim 1. Similarly, for the reasons set forth above, Karnauchow fails to teach a section of a glycosylated human CD55 protein having a tumor-specific glycostructure as encompassed by claim 50. Applicants submit that the present claims are free of the 35 U.S.C. § 102(b) rejection over Karnauchow. This basis of rejection should be withdrawn.

Finally, Applicants note that Karnauchow fails to teach the specific embodiments of the present invention encompassed by claim 43 and new claim 51. Claims 43 and 51 require that the glycoprotein, if present on a cell and bound by an antibody specific for said glycostructure, results in apoptosis of the cell. Karnauchow does not describe EVR1 inducing apoptosis of HeLa cells or of cells recombinantly expressing DAF (CD55). In

fact, Karnauchow teaches that EVR1 can bind to HcLa cells and protect them from Enterovirus 70 infection (see the Karnauchow abstract). As Karnauchow does not teach the every feature of the invention of claims 43 and 51, this reference cannot anticipate these claims.

CONCLUSION

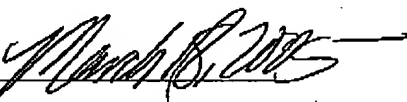
Applicants submit that the application is now in condition for allowance and this action is hereby respectfully requested.

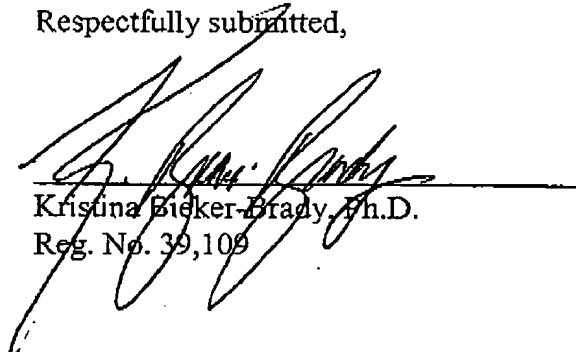
The undersigned hereby respectfully requests a telephonic interview with the Examiner to discuss the arguments set forth in the present reply once the Examiner has reviewed these arguments.

Enclosed are a Petition to extend the period for replying to the Office Action for one month, to and including March 18, 2005, and an authorization to charge the required extension fee to Deposit Account No. 03-2095. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date:




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